A study on profile of ingestional hair dye poisoning

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A STUDY ON PROFILE OF INGESTIONAL HAIR DYE POISONING

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CERTIFICATE

This is to certify that this thesis entitled "**A Study on Profile of Ingestional Hair Dye Poisoning"** is a bonafide work of **Dr P Shridharan** for the degree of M.D. General Medicine under my guidance and supervision.

The method of work and the results embodied have been checked by me time to time and are contributory to the knowledge of the subject.

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DECLARATION

I, **Dr P Shridharan,** declare that, I carried out this work on, "**A Study on Profile of Ingestional Hair Dye Poisoning**" at the Department of Medicine, Govt. Rajaji Hospital during the period of July 2012 to December 2012. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any other University, Board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine.

Place : Madurai Dr P Shridharan

Date :

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CONTENTS

INTRODUCTION

1. INTRODUCTION

Poisoning comprises an important proportion of cases admitted in the medical wards of our hospital. Poisoning is one of the preferred means of suicide / self harm. Poisoning either due to intentional, deliberate self harm or by accident may cause significant morbidity and mortality, and also significant social consequences.

Insecticides, especially organophosphorus compounds comprise the major chunk of self harm or suicidal cases admitted in the hospitals. Of late, people resort to novel modes of attempt to self harm in the changed sociocultural scenario.

The overall suicide rate due to self poisoning was about 31% in South India [2]. The highest rates of poisoning was due to household agents, drugs, insecticides, chemicals, animal or reptile bites in the descending order of frequency [1]. Among the house hold articles used for self harm - drugs (prescribed for other medical or surgical conditions for self or for others), chemicals (lavatory cleaners, hair dye) are noteworthy. The first case of systemic toxicity due to hair dye - paraphenylene diamine was described in 1924 in a saloon owner. Paraphenylene diamine poisoning is common in Morocco and Arabian countries.

Hair dye ingestion and poisoning, though relatively rare in our setting until a decade back, is now emerging as one of the most important reasons for self harm. The ease of availability in virtually each and every household to hair dye gives the victim an easy chance to consume it.

Para phenylene diamine (PPD), an important constituent of hair dyes is the main culprit in the protean manifestations associated with hair dye poisoning. It is an allergen, causing angioedema with oral, labial, lingual, pharyngeal and laryngeal edema causing acute airway compromise threatening the life of the patient within a few hours of ingestion.

It also causes rhabdomyolysis leading to muscle pain, swelling and tenderness, eventually leading to acute kidney injury, pigment nephropathy. It may also cause myocarditis, hepatitis and other metabolic abnormalities which may threaten the life of the patient.

In the absence of specific antidote and the relative easy availability of the component, a high index of suspicion, early preventive measures are required for a good outcome.

Case reports regarding ill effects of paraphenylene diamine has been reported in many international and national journals. As the incidence of paraphenylenediamine poisoning is increasing in our hospital, an attempt is made to study the profile of patients admitted with ingestional hair dye poisoning GRH.

REVIEW OF LITERATURE

2. REVIEW OF LITERATURE

Hair Dye and its ingredients

Permanent hair coloring is done by the use of oxidation dyes. These are composed of para phenylene diamine, a coupling agent and an oxidant. Oxidizing agents are primarily hydrogen peroxide. Coupling agents are usually derivatives of aniline. The mechanism of coloring of hair involves three steps i.e., oxidation of p-phenylene diamine derivative to the quinine state, reaction of the resultant compound with a coupler, oxidation of the resulting compound to the final dye [3].

The brand most commonly used in our setting is SV 33, which has the following ingredients – paraphenylenediamine 4%, propylene glycol, liquid paraffin, cetostaeryl alcohol, resorcinol, ethylene diamine tetra acetic acid, sodium lauryl sulphate, preservatives and perfumes [7]. P-phenylene diamine is also present in most other hair dye brands like Gj, Kk, Cm etc. it is available both in liquid and powder form.

The major toxic component of hair dye causing protean manifestations is paraphenylene diamine(PPD). Propylene glycol and resorcinol may also cause toxic effects.

Propylene glycol

Propylene glycol also plays a significant role in the morbidity of hair dye ingestional poisoning patients. It is a viscous colorless liquid used as a solvent. It has the propensity to cause metabolic acidosis, hyperosmolarity, CNS depression, arrhythmias, and plays add on role in the causation of renal dysfunction in some cases.

The characteristic features of ppd poisoning namely rhabdomyolysis and airway edema is characteristically absent in pure propylene glycol poisoning [7].

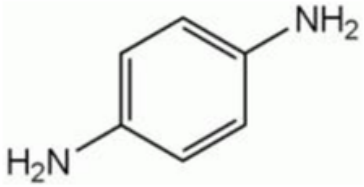
Resorcinol

A constituent of hair dyes, it is postulated to cause renal failure, but no concrete studies are available.

PARAPHENYLENE DIAMINE

It is a derivative of aniline. It is an organic compound with chemical formula of $C_6H_4(NH_2)_2$. It is also known by 4 phenylene diamine, 1,4 – phenylene diamine, 4 – benzne diamine, 1,4 – benzenediamine, para diamino benzene, para amino aniline etc., This compound darkens due to air oxidation.

Apart from hair dyes, PPD is found in shampoos, conditioners etc. p-phenylene diamine is also used extensively in other fields like reduction of rubber products, developing agent in color photographic film development process and so many other related industries.



structure of paraphenylene diamine

PPD is declared as a contact allergen by the Centers for Disease Control, USA. It is a brown or black colored solid, which is soluble in hydrogen peroxide and is not soluble in water. It is a good hydrogen donor. It is metabolized by cytochrome p 450 peroxidase to an active radical forming a reactive compound called benzoquinone diamine. It is further metabolised to a compound knowm as Brandowaski's base.

Brandowaski's base has the propensity to cause anaphylaxis and is strongly mutagenic. It is traditionally used in coloring palms, soles. It is added with henna to dye the hair. The concentration of p-phenylenediamine in these products varies from two to ten percentage. Exposure to p-phenylenediamine occurs through inhalation, skin contact, eye contact and ingestion.

The first case of systemic toxicity was described by Nott[4] in 1924. In India, systemic toxicity of hair dye (p-phenylene diamine) was first documented and published by Chugh et al and Sood et al [5].

Systemic toxicity of paraphenylene diamine

Systemic toxicity may occur due to suicide, accident or homicide. It is also used as an abortifacient. Skin and eye contact causes skin irritation, contact dermatitis, lacrimation, chemosis. It may also cause exophthalmos, or even permanent blindness due to local contact. The lethal dose is estimated to be seven to ten grams in various studies [6].

In the acute phase, which is about four to six hours, ppd causes local effects such as burning sensation and numbness in the mouth, burning and choking sensation in the throat, abdominal pain predominantly in the epigastric region, vomiting which may cause dehydration and aspiration, dysphagia, dysphonia due to swelling of the tongue, sublabial structures, and

of the larynx and pharynx which may ultimately lead to airway obstruction, respiratory failure with resultant hypoxia, cyanosis leading to altered sensorium, neurological manifestation like seizures mainly due to hypoxia and even death due to respiratory arrest and neurological complications if unattended. Exophthalmos, optic neuritis and permanent blindness has also been reported in some studies. Intervention in this acute phase is crucial in the outcome of the poisoning .

The interventions advised namely steroids, prophylactic tracheostomy and adequate hydration help to overcome the acute stage of this condition while also simplifying the need for vigorous treatment in the subacute, chronic phase. Ventilator support may be needed in this condition.

The second phase following the acute phase which manifests itself in days to weeks is characterized by muscle pain, muscle swelling and tenderness due to rhabdomyolysis which usually manifests by 10 to 12 hrs after ingestion of hair dye [8].

Rhabdomyolysis causes muscle necrosis and myoglobinuria, with the myoglobin clogging the renal tubules and causing acute tubular necrosis leading to acute renal failure. Urine discoloration to brown or black due to excretion of the dye, which should be picked up early and treated vigorously

with immediate and liberal intravenous fluids to flush out the dye and myoglobin should be carried out to prevent renal damage. Additionally the urine can be alkalinized with the help of sodium bicarbonate to make the myolglobin and dye excretion easier should be carried out [6].

Kidney damage occurs not only due to rhabdomyolysis with ensuing pigment nephropathy but is also caused/aggravated by hypoxia, dehydration, intravascular hemolysis and a possible direct toxic effect of the dye on the kidney. Renal replacement therapy ie., dialysis may be necessary in some patients in whom these measures fail to prevent or revert renal failure.

Urine examination may show hemoglobinuria, albuminuria, myoglobinuria, proteinuria etc.; p-phenylenediamine can be detected in urine by thin layer chromatography on silica gel, sprayed with 0.2% solution of potassium dichromate as a chromogenic reagent to give a pinkish brown color [8].

Blood biochemistry may show elevated urea, creatinine, dyselectrolytemia, elevated creatine phosphokinase, ALT, AST etc., Elevation of transaminases may be due to liver damage per se or more commonly may be due to muscle damage.

Para-Phenylene Diamine may also cause hepatitis, myocarditis etc. Myocarditis, though occurring in a small percentage of individuals is a

potentially lethal complication with high mortality even if treated adequately. Clinical manifestations of myocarditis varies – may be asymptomatic to fatal. The common clinical features are tachycardia, tachypnea, dyspnea, chest pain, syncope; ecg changes may range from sinus tachycardia, ST-T changes to heart blocks, atrial and ventricular ectopics, atrial fibrillation, ventricular tachycardia and fibrillation. It is diagnosed with the above said symptoms, ecg changes, cardiac biomarkers (troponin T and CPK MB) elevation and echocardiography showing dilated ventricles and reduced ejection fractions [8]. Reports of myocardial infarction due to p-phenylene diamine poisoning has also been reported [9].

Other laboratory abnormalities include anemia, leucocytosis, hypocalcemia, increased C reactive protein, decreased C3 & C4 etc., [10]

The diagnosis is sometimes complicated if the patient doesn't divulge what he/she has consumed and the attenders were not aware of the ingestion. In these times characteristic clinical features namely angioedema of the face, neck, tongue and sublabial structures, dark colored urine, muscle pain and swelling indicative of rhabdomyolysis , urine sediments especially myoglobin, proteinuria with elevated renal parameters in the blood and most importantly elevation of CPK is helpful to arrive at the diagnosis.

Treatment is mainly supportive. No specific antidote is available.

cervicofacial edema produced by PPD poisoning

The short term prognosis is determined by respiratory failure. The long term prognosis is related to muscle and kidney damage. Prevention of acute renal failure with liberal fluid infusion, urine alkalinisation and maintaining good hemodynamic status is an important aspect of the management of PPD poisoning because it is associated with high mortality [8].

Rhabdomyolysis

Destruction of skeletal muscles and the consequent release of pigments especially myoglobin may cause acute renal injury. There are a variety of causes of rhabdomyolysis.

The causes of rhabdomyolysis [11] may be grouped into (i)Genetic Diseases/Disorders (ii) muscle damage (iii) Drugs/Toxins (iv) increased Muscle Activity (v) infections

(vi) Ischemic Conditions

(vii) Dyselectrolytemia

(viii) Endocrine/Metabolic Disorders

(ix) Immunologic

Pathogenesis of rhabdomyolysis : Impairment of normal sequestration of calcium in the sarcoplasmic reticulum in the muscles which occurs due to disruption of the skeletal muscle cell membrane - intracellular calcium overload ensues, which is often aggravated by decreased ATP. Increased intracellular Ca causes lethal effects ie., myofibril and membrane damage – which eventually leads to death of skeletal muscle cells with consequent lysis and release of the intracellular contents (myoglobin) into the circulation.

Dyselectrolytemia occurs due to the release of potassium and phosphate leading to hyperkalemia and hyperphosphatemia which may aggravate the clinical picture. This is compounded by hypovolemia which increases the chance and severity of kidney injury.

Drugs/toxins cause rhabdomyolysis by several mechanisms [11]

- increased muscular activity (eg., phencyclidine)
- drug induced hyperthermia (eg., halothane)
- limb ischemia secondary to arterial involvement (eg., cocaine)

- decreased ATP production (cyanides)
- K+ or phosphorus depletion (diuretics)
- myositis due to hypersensitivity
- direct toxicity (alcohol);
- in addition to these, coma caused by drugs eg. alcohol, cocaine may cause muscle compression, ischemia and consequent rhabdomyolysis.

Other drugs associated with rhabdomyolysis include – barbiturates, amphetamines, benzodiazepenes, suxamethonium, propofol; Snake venom, especially of the sea snakes is an important cause of rhabdomyolysis.

Genetic/Inherited disorders : Decreased energy production due to impaired substrate utilization is the mechanism of rhabdomyolysis in genetic/inherited disorders like Mc Ardle's syndrome due to myophosphorylase deficiency. Phosphofructokinase deficiency, Carnitine palmityl transferase deficiency are also associated.

Infections eg., influenza and leptospirosis can cause rhabdomyolysis by disruption of skeletal muscle cell membrane. Clostridium can be directly myotoxic – gas gangrene [11]. Legionnare's disease, HIV, shigellosis, salmonellosis may also cause rhabdomyolysis.

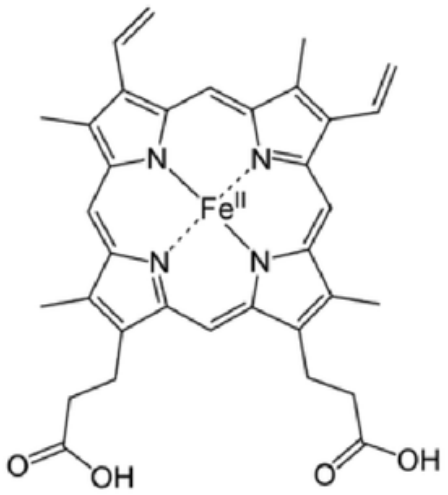
Exertional Rhabdomyolysis : Excessive, especially unaccustomed muscular activity can lead to rhabdomyolysis. Aggravating conditions include fasting, pre existent muscle injury, hypovolemia, working in a hot environment etc. it is especially common in 'de conditioned' persons. The mechanism is early depletion of energy reserves in the muscle leading to impaired membrane transport of calcium leading to intracellular Ca accumulation with consequent effects. Seizures/status epilepticus, tetanus may also cause a similar picture [11]

Metabolic causes : Hypokalemia causes blunted vasodilatory response during exercise leading to muscle ischemia and consequent rhabdomyolysis. Hypo and hyperthermia, hypophosphatemia, hypothyroidism are the other significant causes of rhabdomyolysis [11]

Myoglobin [12]

Myoglobin is composed of globin and heme, weighs about 17800 daltons, one fourth of the weight of hemoglobin. It is a single polypeptide chain with 152 aminoacids. Mb has higher affinity to oxygen than that of hemoglobin though it binds to only one molecule of oxygen.

It has been described as an 'oxygen storage protein' in muscle. Its serum half life is 1 to 3 hours. Small amounts of myoglobin are cleared by the reticuloendothelial system in normal conditions.



myoglobin structure

Myoglobin content of skeletal muscles is 2.5 g/100g; cardiac muscle has 1-4 g%.

The normal unbound fraction of myoglobin is usually 15 to 50 percentage. Myoglobin is visible in urine to the naked eye when the urinary concentration is moe than or equal to 100 mg percent. Levels as low as 0.5 mg percentage can be detected in urine by benzidine, orthotoluedene or guaiac tests. But these tests are not specific and may be false positiive in

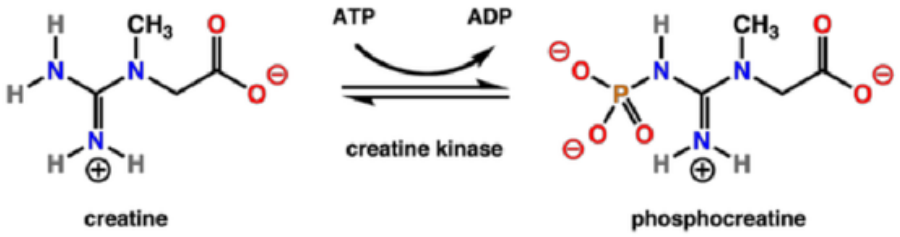
hemoglobinuria. In these situations, spectrophotometry and immunodiffusion is helpful.

Because of the rapid renal clearance of myoglobin, ie., 1 to 6 hours, it may not be always positive if the patient is tested, after long periods following ingestion of ppd. In these situations, creatine kinase which has a longer half life (1.5 days) may be helpful.

Creatine phosphokinase [12]

Also known as creatine kinase, this enzyme is expressed by various issues/cell types. It is a protein product of chromosome 19, with a molecular weight of 86000. CPK is a dimer of two subunits – these may be B or M. Therefore, it exists in three isoenzyme forms namely MM, BB, MB.

Isoenzyme	Electrophoretic mobility	Tissue of origin	Mean percentage in blood
MM	least	Skeletal muscle	90%
MB	intermediate	heart	9%
BB	maximum	brain	1%



Creatine Kinase catalyses the conversion of creatine to phosphocreatine. It serves as an energy reservoir in spermatozoa, smooth muscle, muscle, brain, retina, etc. by rapid buffering and regeneration of adenosine triphosphate in situ. Normal serum value for CK is 20-80 iu/l for males and 20-50 iu/l for females.

Creatine Kinase may be elevated pathologically in myocardial infarction, muscle injury, myositis, myocarditis, statin medications etc.

CK elevations can be seen in the normal population in the following settings – trauma, muscle cramps, intramuscular injections, needle electromyography, vigorous exercise etc. [13]

CK elevation in muscle disease is due to myonecrosis or membrane defects. Highest elevations are seen in rhabdomyolysis, dystrophinopathies, severe polymyositis and neuroleptic malignant syndrome. Modest elevation is seen in myotonic dystrophy and inclusion body myositis. Not all myopathies

have elevated CK. Myopathies with normal CK levels include – mitochondrial myopathies, channelopathies, hyperthyroidism associated myopathy and steroid induced myopathy – in these conditions there's no damage to the muscle cell membrane leading to normal CK levels. Inflammatory myopathies (polymyositis) on steroids may have normal CK levels. Likewise, in muscular dystrophy, in the late stages, due to loss of muscle mass and strength, CK levels may be normal.

CK elevations may also be seen in amyotrophic lateral sclerosis, guillian barre syndrome and spinal muscular atrophy [(14)]. In these conditions, the elevation is usually less than 5 times normal.

Asymptomatic increased levels of CK is seen in acute MI, drugs, trauma, hematoma, IM injections - in the descending order of frequency in a study conducted by Austrian Medical Service[(15)] ; A persistent unexplained CK elevation in otherwise normal healthy individuals in whom the usual causes of elevation are excluded is termed 'Idiopathic CKemia' [(16)].

CLAM (cholesterol lowering agent myopathy) is a condition caused by statins. They may cause asymptomatic CK elevations or myalgias or even rhabdomyolysis. The postulated mechanism is that statins causes unstable myocytes by lowering the cholesterol content inside the myocytes[(17)].

In myocardial infarction, CK MB fraction starts to rise within three hours of infarction. Therefore CK estimation is very useful in detecting early cases. CK returns to normal levels in almost 24 hours after myocardial infarction. Thus, it is useful in detecting re infarction after 24 hrs; Troponin T which is considered superior to Creatine Kinase in diagnosing myocardial infarction cannot be relied upon to diagnose re infarction because of the fact that it remains elevated for almost 5-7 days post infarction [12]. Since CK MM fraction comprises almost 90% of the total CK, muscle disorders can be confidently diagnosed by the total fraction alone. Lowered CK is seen in alcoholic liver disease and rheumatoid arthritis.

CK is a more sensitive marker of muscle injury than myoglobin because it is cleared slowly. Several reports have established that increased CK levels are found in patients with renal failure than for those who do not have renal failure[21]. Increasing or decreasing creatine kinase indicates worsening or resolving rhabdomyolysis respectively; hence CK levels should be monitored serially when the patient is in the hospital.

Acute Kidney Injury

It is defined as rapid decrease in the glomerular filtration rate (within hours to weeks) associated with the retention of nitrogenous waste products ie., blood urea nitrogen and creatinine.

Oliguric AKI denotes urine output less than 400 ml/day, non oliguric AKI denotes output more than 400 ml/day and anuric means output less than 100 ml/day[24].

Prerenal AKI is one in which the renal parenchymal integrity is preserved. It is characterised by renal hypoperfusion due to a variety of causes. Intrarenal or intrinsic AKI denotes damage to the parenchyma of the renal tissue. Obstruction of the urinary tract leading to renal failure comes under Postrenal or Obstructive AKI.

The hallmark of acute tubular necrosis is tubular injury. It affects the outer medulla of the kidneys usually - especially the proximal tubule and the ascending limb of loop of Henle[24]. Nephrotoxins cause ATN by several mechanisms which include direct toxicity, intratubular obstruction, intrarenal vasoconstriction.

The kidneys are more vulnerable to nephrotoxins due to the following reasons –

i) concentration of toxins within the medullary interstitium

ii) rich blood supply – almost 25% of the total cardiac output

iii) transformation of compounds into toxic metabolites.

iv) In addition, the injury may be accelerated or complicated by hypovolemia, sepsis etc. About 30% of rhabdomyolysis cases can develop renal failure[24].

Intrinsic renal failure may be due to

- the affection of blood vessels (conditions affecting the renal arteries and/or veins)
- disorders of the glomerulus & the microvasculature (malignant hypertension, hemolytic uremic syndrome, allograft rejection etc.,)
- tubulointerstitial diseases (allergic interstitial nephritis due to certain drugs, infections, infiltrations like leukemia etc.,)
- predominant renal tubular injury (ischemia by hypoperfusion, exogenous toxins like drugs, endogenous toxins like hemoglobin, myoglobin etc.,)

Myoglobinuric acute kidney injury – Pathophysiology

The pathophysiology of renal failure is probably multifactorial in rhabdomyolysis. The following factors [11] cause acute kidney injury in myoglobinuria –

- Tubular obstruction due to pigment deposition
- Glomerular fibrin deposition
- Hypovolemia leading to renal ischemia
- Direct renal tubular toxicity

Renal vasoconstriction occurs due to augmented sympathetic activity and renin angiotensin activity, decreased nitric oxide and prostaglandin production[11]. Heme proteins are thought to scavenge NO, which is an important endogenous vasodilator. Renal ischemia and oxygen intermediates both play an important role in the pathophysiology of myoglobinuric renal failure.

Myoglobin is more toxic to the kidney in the setting of academia and hypovolemia[11]. There is an initial decrease in GFR and low fractional Na excretion in rhabdomyoltic renal injury. Volume expansion when given after

18 hours of onset of rhabdomyolysis is unlikely to help because of the possible tubular necrosis that has set in by the time.

In the presence of acidic tubular fluid, myoglobin is converted to ferrihemate which is directly toxic to tubules[18]. The heme moiety is the nephrotoxic factor in myoglobinuric renal injury. Heme sensitizes the tubular cells to damage by phospholipase A2. Also, heme is thought to deplete cellular energy stores[11].

The mere presence of myoglobinuria may not cause acute renal failure; other co existing conditions like hypovolemia and acidic urine is required to cause the same[11]; this gives a rationale for early infusion of large volume of fluids and alkalinisation of urine to hasten recovery/ prevent renal injury in rhadomyolysis.

Tubular obstruction by cellular debris and pigmented casts causes tubular epithelial injury[24]. Both hypovolemia and acidemia accelerate this process. Increased urinary uric acid is also seen in rhabdomyolysis leading to uric acid precipitation[11]. Tubular obstruction causes decreased glomerular transcapillary hydraulic pressure and release of thromboxane which cause reduction in glomerular filtration rate[19].

Glomerular microthrombi deposition also contributes to the development of renal injury in myoglobinuria because of the propensity to initiate disseminated intravascular coagulation[20].

Clinical and laboratory features of rhabdomyolysis and acute renal failure

Patients may complain of muscle pain, swelling of limbs etc. On examination muscle tenderness may be found. Relevant history to ascertain the exact cause ie., trauma, drug intake, pigment nephropathy should be taken. The incidence of renal injury in rhabdomyolysis ranged from 5% to 33%. [11]

Patients at high risk for development of renal injury following rhabdomyolysis include those with [11]

- elevated serum creatinine
- hypertension, hypotension
- hypovolemia
- older age
- higher serum potassium and phosphorus levels
- lower levels of calcium and albumin

- low urinary pH

URINE is usually dark, and acidic. Urinalysis shows nil RBCs or less than 5 per hpf. The benzidine or orthotoluidene test gives a positive result. Proteinuria may be present – reflecting glomerular injury or tubular transport of small proteins. Pigmented brown granular casts and renal tubular epithelial cells are also seen in microscopy.

The differential diagnosis of pigmenturia includes hemoglobinuria, myoglobinuria and porphyria which can be differentiated by various methods as follows [11].

Differential diagnosis of pigmenturia

Factors	Porphyria	Hemoglobinuria	Myoglobinuria
Urine color	Dark red	Reddish brown	brown
Serum color	clear	pink	clear
Muscle pain, tenderness	absent	absent	Present
Serum creatine kinase level	normal	normal	elevated
Serum haptoglobin	normal	decreased	normal
Orthotoluidene reaction	negative	positive	positive
Watson-schwartz porphobilinogen	positive	negative	negative

An increased anion gap acidosis is usually found in patients of rhabdomyolysis who progress to renal failure. Acidemia may occur due to 2 mechanisms – retention of inorganic anions eg., phosphate, and defective renal excretion of acids produced by muscle injury.

Hyperuricemia is common in patients with rhabdomyolysis, especially due to muscle injury. Damaged muscles release intracellular purines which in turn is converted by the liver to uric acid leading to hyperuricemia.

The rise of serum creatinine compared to serum blood urea nitrogen is more in cases of renal failure due to rhabdomyolysis than due to other causes. This is because muscle injury releases creatine which is converted to creatinine[11].

Hyperphosphatemia occurs in muscle injury due to the release of intracellular phosphate into the circulation. It is further aggravated by the fact that the excretion of phosphate is defective because of acute renal failure.

Hypocalcemia also occurs in the setting of myoglobinuric renal injury. Calcium is deposited in the muscles in the oliguric phase of renal failure. Hyperphosphatemia also contributes to hypocalcemia. Hypocalcemia may also be due to the disturbances in the vitamin D, parathyroid hormone

metabolism. Reduced synthesis of vitamin D and relative resistance to the action of vitamin D have been found[22].

Hypercalcemia also occurs in the course of myoglobinuric renal injury. This is seen especially during the recovery phase of renal failure[11].

High fractional excretion of sodium occurs due to the fact that the renal tubular reabsorption of sodium is defective in the setting of oliguric renal failure.

DIC : muscle damage leads to release of intracellular thromboplastins resulting in the activation of clotting cascade and development of disseminated intravascular coagulation[23].

Differential diagnosis

Myoglobinuric AKI is suspected in the setting of classic triad – positive urine test, dark discoloration of urine, elevated serum CK levels. Drugs such as rifampin, nitrofurantoin, pyridium, sulfa compounds etc. may cause discoloration; porphyrias can also discolor the urine. These can be differentiated by benzidine or orthotoluidene test.

Clinical course and complications of myoglobinuric acute kidney injury

Renal dysfunction may be mild characterized by oliguria only for a few days followed by rapid recovery or it may be sever requiring dialysis for few weeks. Oliguria if persists may last for 7 to 10 days. Peripheral neuropathy may also occur due to compartment syndrome. Urgent fasciotomy may be required in this situation.

Prevention and treatment of myoglobinuric acute kidney injury

The cornerstone of management of renal failure in this condition is prompt recognition of the cause as myoglobinuria and constitution of adequate and liberal hydration to ensure high urinary flow rate and also alkalinisation of urine to accelerate the excretion of the pigments to prevent or mitigate the renal injury[24].

Alkalinisation of urine

Drugs and toxins' elimination via kidney depends upon the following factors – the degree of protein binding, tubular secretion of the drug/toxin, energy dependent tubular reabsorption[24].

Alkalinisation and acidification are two processes done to hasten elimination of drugs or toxins. The goal is to increase the ionized portion of

the specific toxin which may be a weak base or weak acid –thereby preventing the passive tubular reabsorption of the same leading to easier elimination.

A drug is amenable to urinary alkalinisation if it fulfills the following conditions –

a) should be excreted unchanged by the kidney

b) low level of protein binding

c) extracellular distribution

d) weakly acidic with a dissociation constant of 3 to 7.5

Since myoglobin is thought to be more nephrotoxic in acidic pH (due to increased ferrihemate formation), early and vigorous administration of large volume fluids having sodium salts of citrate, bicarbonate, lactate significantly decrease mortality rates[24].

Before initiating alkalinisation, in addition to the routine investigations, urinary and arterial pH and serum concentration of the toxin should be assessed. Two to three ampoules of sodium bicarbonate ie., 50 to 150 mEq should be added to one litre of 5% dextrose in water solution or to 0.45% saline.

The initial rate of infusion should be adjusted according to the volume status of the patient. Further infusion should be adjusted according to the urinary output of the patient. The desired urine output should be 2 to 3 ml/kg/hour. Urinary catheterisation ensures accurate measurement of output. Serum electrolytes and urinary pH should be checked every 2 to 3 hrs. The desired urinary pH is 7.5 to 8.5. Intravenous diuretics can be used to enhance diuresis[24].

Many studies recommend mannitol as a prophylaxis of acute renal failure in myoglobinuria. Mannitol acts by increasing urinary flow and preventing tubular obstruction by casts, oxygen free radical scavenger, stimulation of prostaglandin release leading to glomerular capillary dilatation, reduces tubular epithelial swelling, increase in glomerular filtration rate due to decrease in oncotic pressure in the glomerulus. It has several extrarenal advantages – ecf volume expansion, reduction of muscle edema and swelling, increased release of atrial natriuretic factor[25].

If the urine flow doesnot improve even after four hours [24] of forced alkaline diuresis, the patient is more likely to go into established phase of oliguric acute tubular necrosis and the treating physician should explore the possibility of instituting renal replacement therapy while continuing conventional measures until dialysis can be arranged.

Complications of alkaline diuresis are fluid overload, pulmonary edema, cerebral edema, hypokalemia. Hypernatremia can occur if free water is restricted.

Cardiac failure, pulmonary edema and cerebral edema are relative contraindications to alkaline diuresis. Plasma exchange and continuous hemodiafiltration have been proposed in some studies to accelerate the removal of myoglobin. But these measures have not been found to be successful[11].

Dialysis

When conservative measures fail to correct the metabolic derangements, renal replacement therapy is indicated.

The principle of dialysis is solute transport and water movement across a selectively permeable membrane. In Hemodialysis, an extracorporeal membrane functions as a selectively permeable membrane. In Peritoneal dialysis, the peritoneal membrane acts as the selective filter. Solute diffusion depends upon the molecular size and concentration gradient; removal of water is termed ultrafiltration. In hemodialysis, the transmembrane hydrostatic pressure helps in removing the excess fluid from blood. In peritoneal dialysis,

water is removed because of the osmotic shift of water towards the hyperosmolar dialysis solution. Common acute indications for dialysis include dyselectrolytemia esp hyperkalemia, refractory volume overload, metabolic acidosis, uremic encephalopathy, intoxications, pericarditis etc. (26).

Peritoneal dialysis for myoglobinuric renal failure

Since myoglobinuric renal failure following p-phenylene diamine poisoning is a highly catabolic state, peritoneal dialysis is inadequate – the rapid rate of solute appearance is much more than the rate of solute clearance – peritoneal dialysis may be woefully inadequate in these circumstances[24]. But in some circumstances such as non availability of hemodialysis in the institution this can be done as a bridge procedure until the patient can be shifted to a center with facilities for hemodialysis.

The complications of peritoneal dialysis - peritonitis, tunnel or exit site infections, outflow failure, fluid leaks, hypokalemia, protein loss etc. should be borne in mind.

Hemodialysis for myoglobinuric renal failure

It is the ideal renal replacement therapy in this condition. Intermittent hemodialysis can ultrafiltrate 3 to 4 liters of fluid in hemodynamically stable

patients[39] Frequency of dialysis in PPD poisoning induced renal failure : most commonly dialysis is required daily usually for the first several days until the urea, creatinine values begin to decrease and the grave consequences of extensive muscle injury abates. Thereafter thrice weekly dialysis is sufficient. Conditions like surgical wound debridement, infection, volume overload may require more frequent dialysis [24]. If therapy is instituted early, full recovery of renal function usually occurs unless complicated by sepsis, bleeding, respiratory failure etc.,

Adequacy of clearance is calculated by urea reduction ratio (URR) which indicates clearance of blood urea nitrogen (BUN). [26]

URR = [(predialysis BUN – postdialysis BUN)/predialysis BUN] x 100

A reduction rate of >65% is considered adequate [26].

Common complications of hemodialysis include infection, intradialytic hypotension, bleeding;

Dialysis Disequilibrium Syndrome - this condition is found in severely uremic patients in the first few sittings of dialysis. Rapid clearance of toxins cause osmotic shifts leading to cerebral edema which is manifested by nausea, vomiting, headache, altered sensorium and seizures. This can be prevented or ameliorated by starting with slower blood flows and shorter treatments.

Myocarditis due to PPD poisoning

Non infective causes of myocarditis include cadiac transplant rejection, giant cell myocarditis, sarcoidosis, polymyositis, dermatomyositis, drugs and toxins like alcohol, cocaine, amphetamine, anthracyclines, trastuzumab etc. (27)

Myocarditis due to para phenylene diamine ingestion can vary from asymptomatic to fatal. Symptoms and signs include dyspnea, tachypnea, presyncope, syncope, tachycardia, hypotension, arrhythmias including ventricular & atrial premature complexes, atrial tachyarrythmias especially atrial fibrillation, ventricular tachycardias, other ecg changes like sinus tachycardia, T wave inversion, ST changes. Cardiac biomarkers like CK MB and troponin T may be elevated. Echocardiography shows reduced left ventricular ejection fractions and regional wall motion abnormality[8,9].

In some studies, the frequency of myocarditis following PPD ingestion was found to be as much as 20% with ecg changes[8]; patients with hypotension, arrhythmias, co existing renal failure and other comorbities had worse outcome.

Treatment includes fluid replacement, vasopressors, DC cardioversion, amiodarone and other antiarrythmics as indicated. Other complications that

are harmful to the heart like hyperkalemia, uremia etc. should b actively sought and treated so as to have a good outcome.

Management of angioedema in PPD poisoning

URTICARIA AND ANGIOEDEMA : Urticaria are raised, flat topped well demarcated skin lesions which are usually pruritic, with surrounding erythema. An individual lesion typically lasts for minutes to few hours. Angioedema is a deeper lesion with pain and swelling[26]. It lasts for 12 to 48 hours and can accompany about 40% to 50% of patients with urticaria. If angioedema occurs without urticaria drug reaction to angiotensin converting enzyme imhibitors, or hereditary C1 esterase deficiency should be thought of. The final common pathway of both conditions is the release of inflammatory mediators due to degranulation of mast cells or basophils[26].

Angioedema is the primary reason for immediate collapse of the patient due to airway compromise and respiratory failure. Immediate preventive measures should be undertaken to save the airway of the patient - these include anti-inflammatory drugs especially steroids, antihistamines, elective intubation, tracheostomy in cases of established airway blockade with impending respiratory failure.

Tracheostomy : done in conditions where the airway edema precludes endotracheal intubation and the patient is in risk for respiratory failure. It can be done as a day care procedure with local or general anesthesia. An opening is made in the anterior wall of trachea and a channel is constructed between the trachea and skin surface of neck by insertion of a tracheostomy tube. It relieves the upper airway obstruction, decreases the amount of dead space, reduces the resistance of airflow and protects against aspiration.

Complications include primary hemorrhage, injury to blood vessels like jugular veins, injury to recurrent laryngeal nerve, damage to cricoids cartilage, tube displacement, crusting, surgical emphysema, tracheoesophageal fistula, secondary infection etc.,

Tracheostomy tube care is a very important but neglected practice. Care includes cleaning and changing of inner tube, tracheobronchial toilet suction at regular intervals, humidification and prevention of crust formation, physiotherapy to prevent accumulation of secretions.

Steroids : these class of drugs mount a non specific anti inflammatory response, irrespective of the type of injury or insult - it effectively acts by the following mechanisms – decreases capillary permeability, reduces local exudation, decreases phagocytic activity. They suppress all types of allergic

and hypersensitivity reactions. They seem to interfere with the production and action of lymphokines.

Many studies have advocated use of hydrocortisone or methylprednisolone for p-phenylene diamine induced angioedema [8]. Hydrocortisone has a short duration of action with principal glucocorticoid activity with a little mineralocorticoid activity. Methylprednisolone is slightly more potent glucocorticoid than hydrocortisone with negligible mineralocorticoid activity. Hydrocortisone is given in dose of 200 mg iv stat followed by 100 mg iv 6^{th} hrly. It is given for 5 days. Methyl prednisolone is given in a dose of 1 gm iv infusion for 5 days. Both these drugs have been shown to hasten recovery and improve mortality and morbidity in hair dye induced angioedema.

Studies done on Profile of ingestional hair dye poisoning patients

- A prospective study was done in Northern India by P K Jain et al, Dept of Medicine, MLB Medical college, Jhansi UP. Published in Janary 2011 in Journal of Clinical Medicine and Research,. it involved 1020 cases over a five year period from 2004 to 2009. In that study majority patients were females, the mortality rate was around 15% . The study

also gave details about the biochemical parameters, treatment modalities used and morbidity data.

- Raghu Kondle et al conducted a prospective study in hair dye ingestional poisoning patients admitted in Narayana Medical College Hospital, Nellore, Andhra Pradesh over e three year peiod. The study included 50 patients. In this study female patients constituted 82%, mortality rate was 4%, seizures were present in 4%, hepatitis was present in 100%, acute renal failure was found in 6%, ventilatory support was required in 48%
- The Journal of Association of Physicians of India in 2009 published a study performed by Manisha Sahay et al, Osmania medical college, Hyderabad. The study was titled 'Hair Dye Ingestion – an uncommon cause of acute renal injury'. In that study 30 consecutive patients with hair dye induced renal failure were studied. All patients had oliguria and fluid overload. Renal biopsy was done in 15 patients which showed acute tubular necrosis. Overall mortality was 26.6%.
- Ajay Paul Singh et al published a case report of hair dye induced myocarditis, of patients admitted in a Gwalior hospital, which was published in Indian Heart Journal, 2009; 61:306-307 The cases showed ecg changes of ST, T wave depression, ventricular extrasystoles etc.

Cardiac biomarkers CK MB, Troponin T were elevated. Treatment was supportive with vasopressors, anti arrythmics and DC cardioversion. The patient also had renal failure. Finally the patient succumbed to the illness.

- Sampath Kumar K et al, Dept of Nephrology, MMHRC, Madurai published case reports of two young women admitted with hair dye ingestional poisoning. Study was published in Indian Journal of Critical Care Medicine 2007. Both patients had rhabdomyolysis, acute renal failure, hepatitis; both were given hemodialysis. Only one of them recovered.
- Sachin S Soni et al conducted a study in Mediciti Hospitals, Hyderabad over a one year period 2006 to 2007, which was published in Indian Journal of Medical Sciences, 2007. The study was conducted in ten patients. The mortality rate was 60%. 6 patients required either tracheostomy or endotracheal intubation for securing airway. The mortality was higher in oliguric patients than in non oliguric patients.
- Arab Journal of Nephrology and Transplantation. 2010 Jan;3(1):39-43 published a study done in a pediatric hospital in Sudan of children admitted after ingestion of hair dye.

- Saudi J Kidney Dis Transplant 1995;6(3):286-289 published a ten year study comprising 150 patients admitted in Khartoum Hospital, Sudan, conducted by Salma Mohamed Suliman et al. All patients had angioedema, 60% had acute renal failure.

AIM OF THE STUDY

3. AIM OF THE STUDY

To study the following in patients admitted with ingestional hair dye poisoning in medical wards of Government Rajaji Hospital, Madurai.

1. Demographic Profile
2. Clinical Profile
3. Laboratory Profile
4. Treatment details
5. Morbidity and mortality data

MATERIALS AND METHODS

4. MATERIALS AND METHODS

Study design

Prospective cross sectional observational study

Study Subjects

Patients admitted in medical wards of Government Rajaji Hospital, Madurai with hair dye ingestion.

Study duration : June to November 2012

Study Setting : Government Rajaji Hospital, Madurai

Ethical Committee approval

Ethical committee approval was obtained to carry out the study

Materials

Of a total of 52 patients admitted with hair dye ingestional poisning in the study period, 46 patients were included in the study.

Inclusion Criteria

Patients admitted with a history of hair dye ingestion with classical symptoms of neck swelling, muscle pain and dark colored urine.

Exclusion criteria

1. Patients and attenders doesn't opt for inclusion in the study
2. Death within 6 hours of admission
3. Absconded within 24 hours
4. Known cardiac disease patient
5. Known renal disease patient
6. Known hepatic disease
7. Patients with history of consumption of other substances/poisons in addition to hair dye.

Study Protocol

Patients admitted in GRH were the study group. A previously designed proforma was used to collect the demographic and clinical details of the patient.

Collaborating Departments

Departments of Biochemistry, Nephrology and Cardiology of Madurai Medical College & Government Rajaji Hospital, Madurai.

Data collection and Methods

Demographic details include age, gender, education, occupation of the individual. Clinical details include cervicofacial edema, limb pain and swelling, discolored urine, oliguria, dyspnea, palpitation, syncope, voice change, pulse and blood pressure data, oxygen saturation in the bedside using a finger pulsoximeter. Laboratory data to be collected include urine analysis for protein, deposits; blood total count, blood urea, creatinine, sugar, serum sodium, potassium, serum total CPK, serum SGOT, SGPT, electrocardiogram, serum cardiac troponin T for patients in whom there are ecg changes and/or symptoms and signs of myocarditis like tachypnea, tachycardia, hypotension etc. Treatment details to be collected include airway management requiring tracheostomy or endotracheal intubation, ventilatory support, the dose, duration and type of steroids used, whether alkaline diereses used, dialysis details if done, the use of vasopressors, antiarrythmics or cardioversion.

Cervicofacial edema, discolored urine, muscle pain & swelling were noted in the first 24 hours of admission. Oliguria, dyspnea, palpitation, syncope, seizures etc were taken into consideration when present anytime during the hospital stay. Urinalysis, blood urea, creatinine, serum electrolytes, serum cpk were taken on admission, the second day and periodically once in

one or two days thereafter. The second – third day values and discharge day values are taken into consideration for the study. ECG was taken for all patients during admission and thereafter only if patient has persistent tachycardia, electrolyte abnormalities, hypotension, dyspnea, tachypnea, chest pain etc. If ecg changes were present, cardiac troponin T was done.

Limitations of this study

- Arterial blood gas analysis was not done due to constraints
- Biopsy of kidney was not done in view of social limitation and in view of the medicolegal nature of all these cases.
- Urine examination for ppd using thin layer chromatography was not done due to constraints.
- Urinary pH estimation was not done
- Abdominal imaging like ultrasound were not done
- CK fractionation was not done due to laboratory constraints
- Urinalysis for myoglobin or hemoglobin eg orthotoluidene test or benzidene test were not done.

Statistical analysis

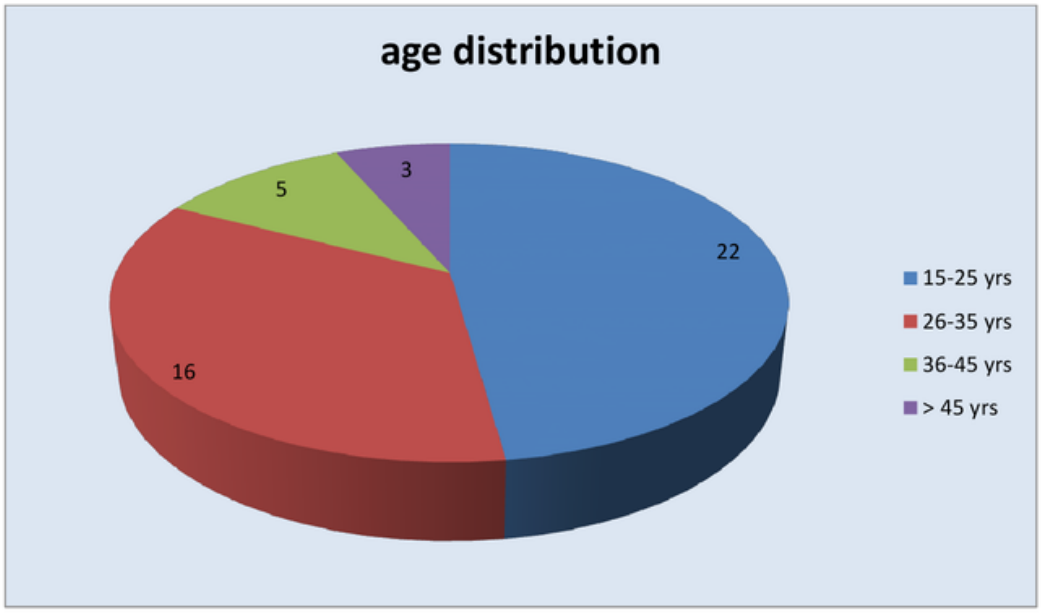
Data analysis was done using epidemiological information package

OBSERVATION AND RESULTS

5. OBSERVATION AND RESULTS

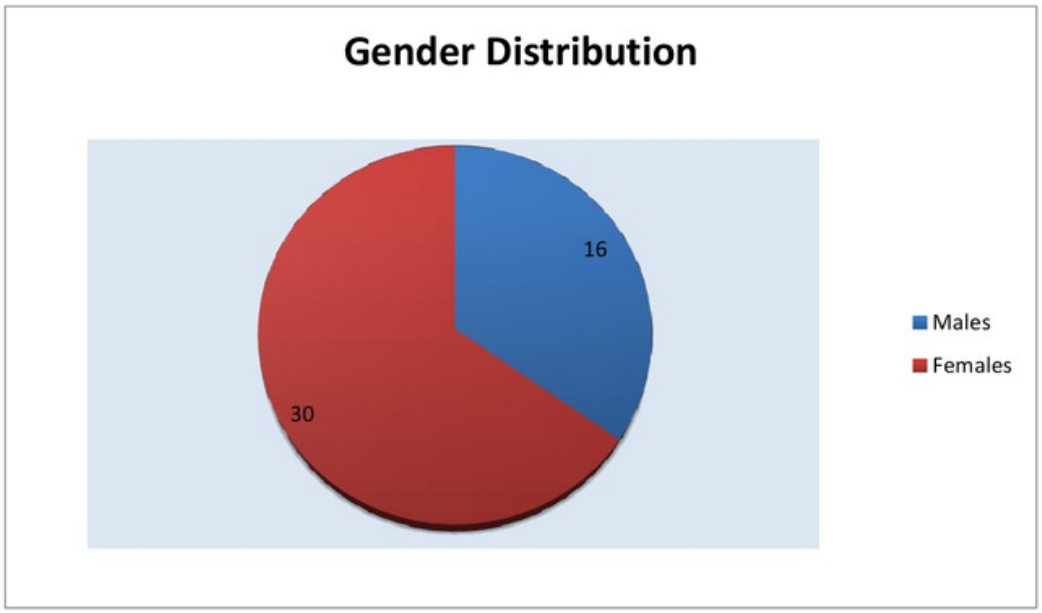
AGE DISTRIBUTION

Age group (years)	Total	Percentage
15 - 25	22	47.8%
26 - 35	16	34.7%
36 - 45	5	10.8%
> 45	3	6.5%
Total	46	100%



GENDER DISTRIBUTION

Gender	No. of cases	Percentage (%)
Male	16	34.78
Female	30	65.22



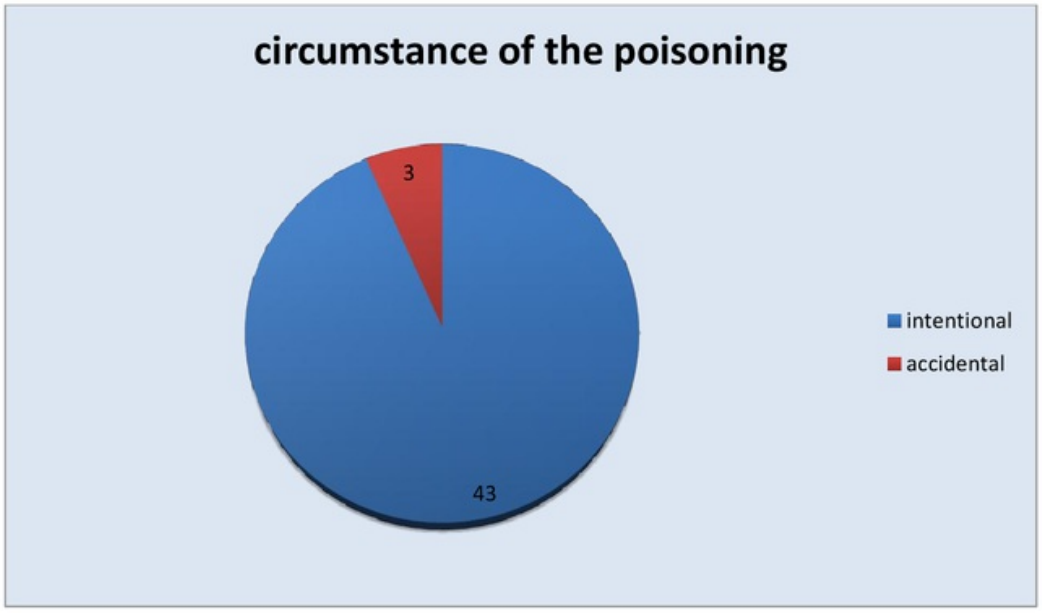
Age and Gender Distribution

Age group (years)	Male	Female	Total	Percentage
15 - 25	4	18	22	47.8%
26 - 35	10	6	16	34.7%
36 - 45	1	4	5	10.8%
> 45	1	2	3	6.5%
Total	16	30	46	100%

The majority of the patients were females, comprising almost two thirds of the cases. In both genders, the 15 to 35 years age group comprised more than 80% of the total number of patients.

Circumstance of the poisoning

Intentional self harm was the reason for 43 out of the 46 patients of the hair dye ingestional poisoning cases in our study. The remainder consumed it accidentally.



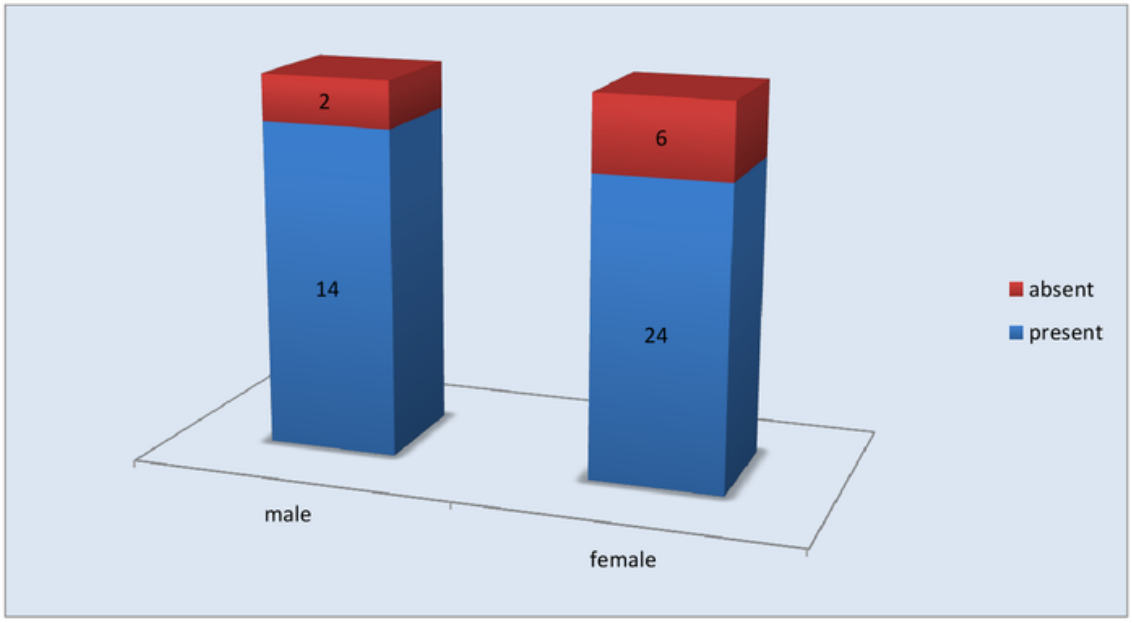
Clinical Features

Sl no.	Symptoms/sign	No. of cases	Percentage (%)
1	Cervicofacial edema	38	82.60
2	Limb pain and/or swelling	37	80.43
3	Brown black colored urine	37	80.43
4	Oliguria	32	69.56
5	Tachypnea, dyspnea	05	10.86
6	hypotension	07	15.21
7	Seizures	01	02.17

About 80% of the patients had angioedema involving the lips, neck, tongue, sublingual structures, pharynx etc. Equal number of patients had discoloration of urine to brownish black color. Muscle pain, swelling is seen in eighty percent of the individuals.

Cervicofacial Edema

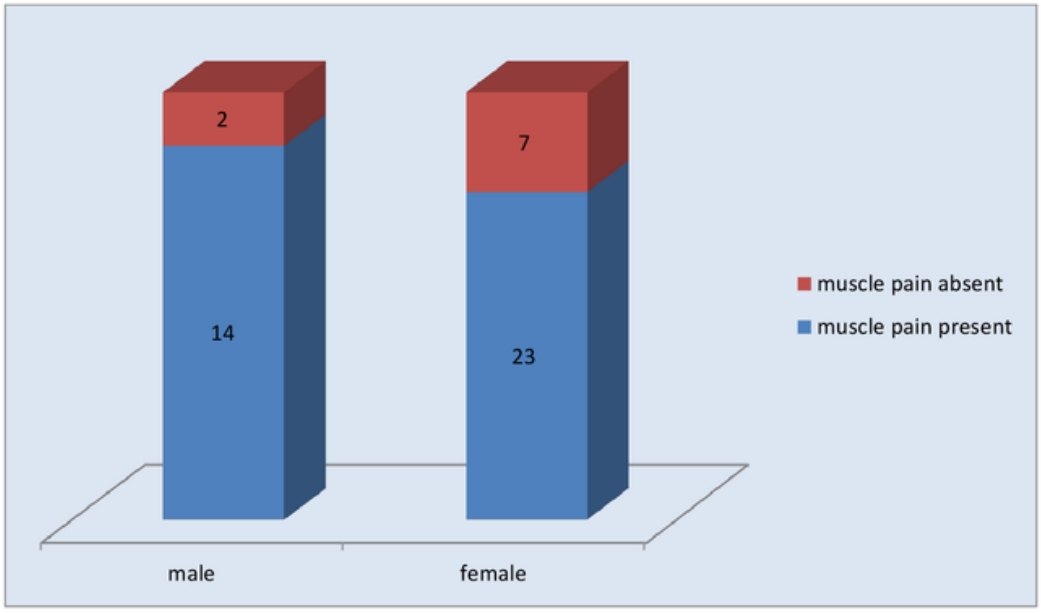
	Male	Female	Total
Present	14	24	38
Absent	2	6	8



Cervicofacial edema, mild to severe, was present in 82.60% of the patients. Among which, males were 36.84% and females comprised 63.16%. Majority of then were managed conservatively, ie., drug therapy, only a small percentage required invasive procedure to maintain/secure the airway.

MUSCLE PAIN & SWELLING

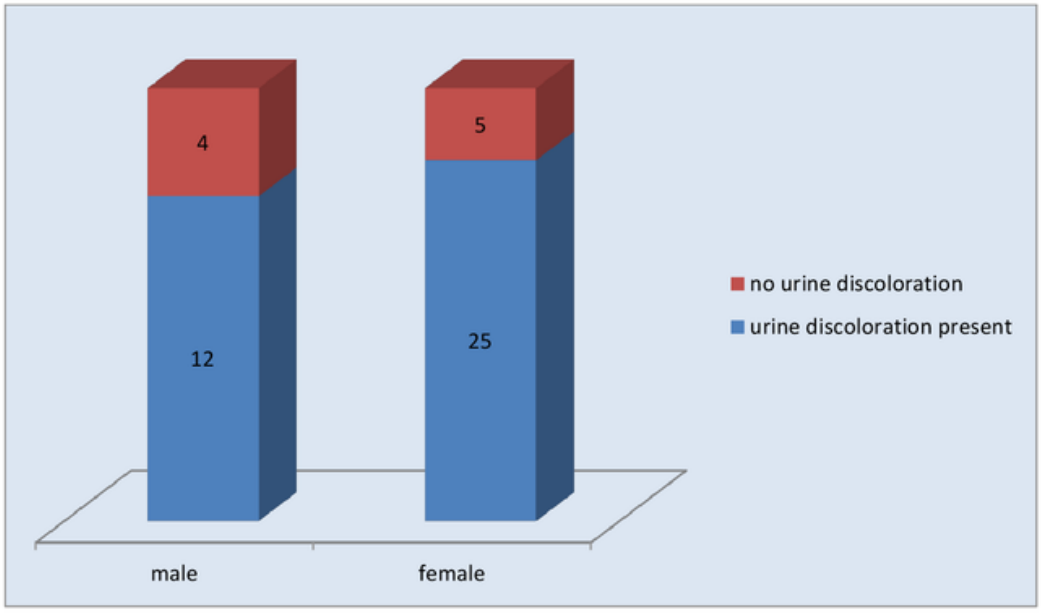
	Male	Female	Total
Present	14	23	37
Absent	2	7	9



Muscle pain, with or without swelling was present in almost 80.43% of the patients of whom 37.83% were males and 62.16% were females. As a whole, 87.50% of males and 76.66% of females had this symptom.

Urine Discoloration

	Male	Female	Total
Present	12	25	37
Absent	4	5	9

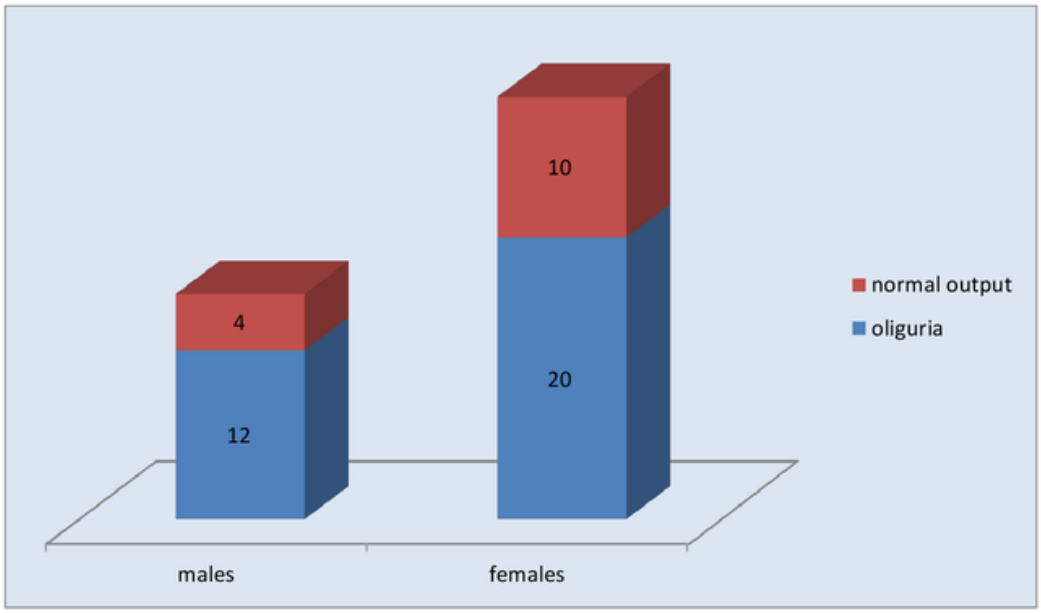


Brownish black discoloration of urine was found in majority of the patients, both male and female.

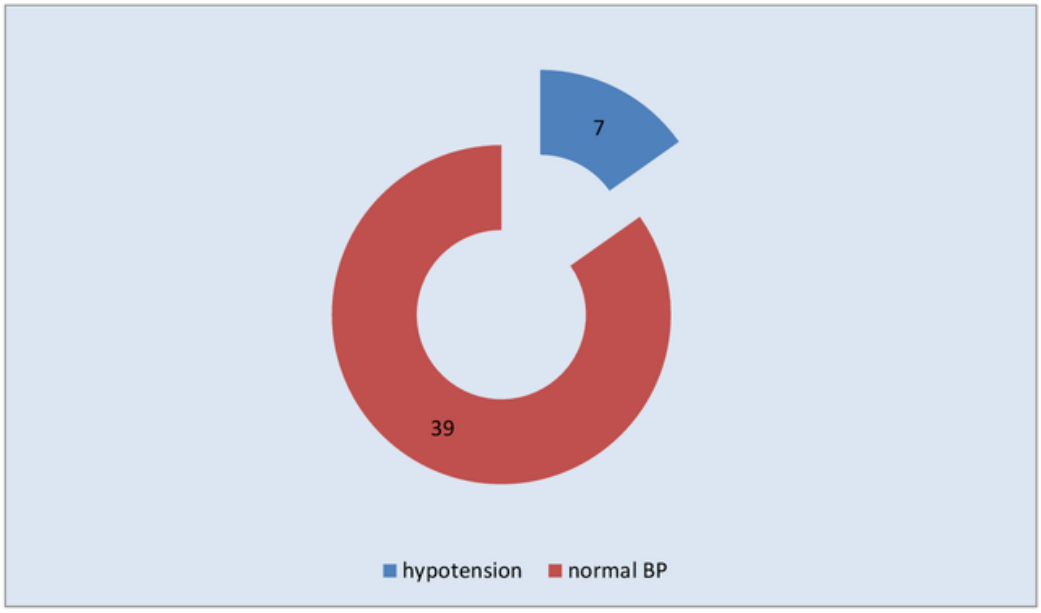
Oliguria

	Male	Female	Total
Oliguria	12	20	32
No oliguria/anuria	4	10	14

69.56% of patients had oliguria; Majority of them recovered with conservative management ie., liberal parenteral fluids and alkaline dieresis within one to two days of admission. Only nine patients required renal replacement therapy.



Hypotension



Only 7 (15.21%) out of the total cases had hypotension. Of these seven patients, only four patients required vasopressors, the remainder recovered with fluid replacement; of the 7 patients who had hypotension, 4 expired – they had other organ system involvement.

Other symptoms/signs

.SEIZURES

Only one patient, a 26 yr old female had seizures, on the 4th day of admission. She had discolored urine, muscle pain, required tracheostomy for maintenance of airway, developed renal failure, required dialysis; eventually she succumbed to the illness. Electroencephalogram was not done since the patient was on ventilator and she succumbed in a few hours after seizures.

Five patients had altered sensorium in the form of drowsiness – they recovered after parenteral fluids, establishment of airway, oxygen and steroid therapy.

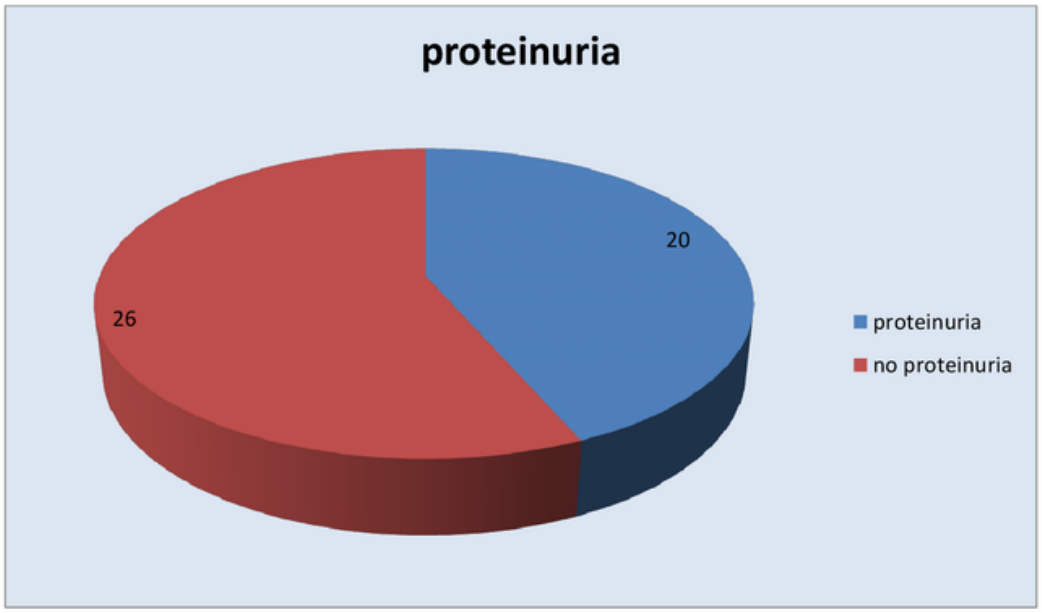
DYSPNEA/TACHYPNEA

Present in five patients out of the total 46 patients.

LABORATORY PROFILE

Urinalysis

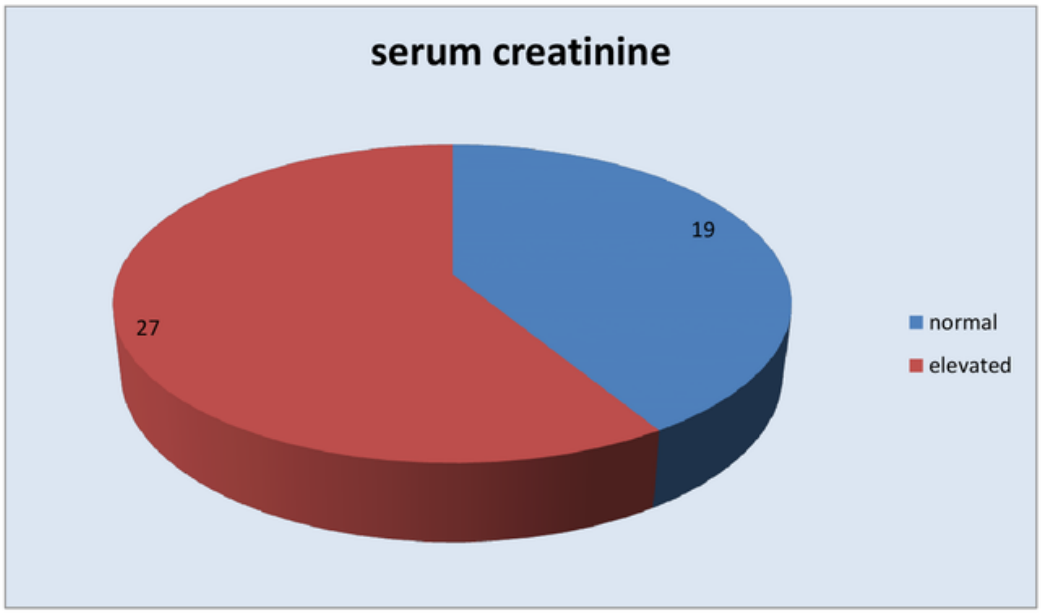
Proteinuria was found in 20 patients, ie., 43.47% of the patients; it ranged from + to +++; it was done by dip stick method



Urine RBCs were found in 12 patients. They were in the range of 1 to 4 RBCs per high power field.

Serum Creatinine

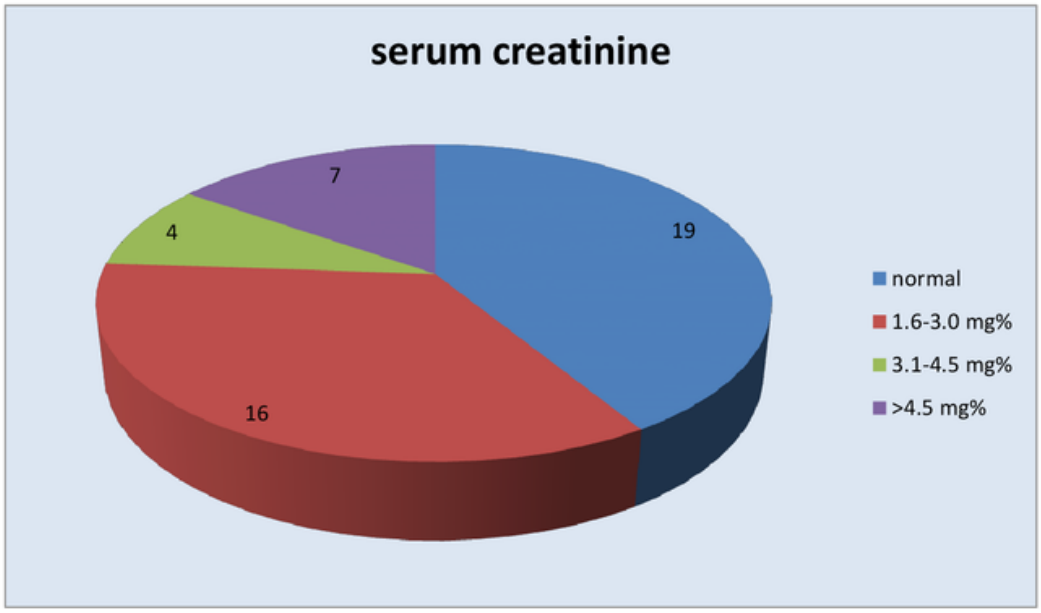
Serum Creatinine	Male	Female	Total
Elevated	8	19	27
Normal	8	11	19



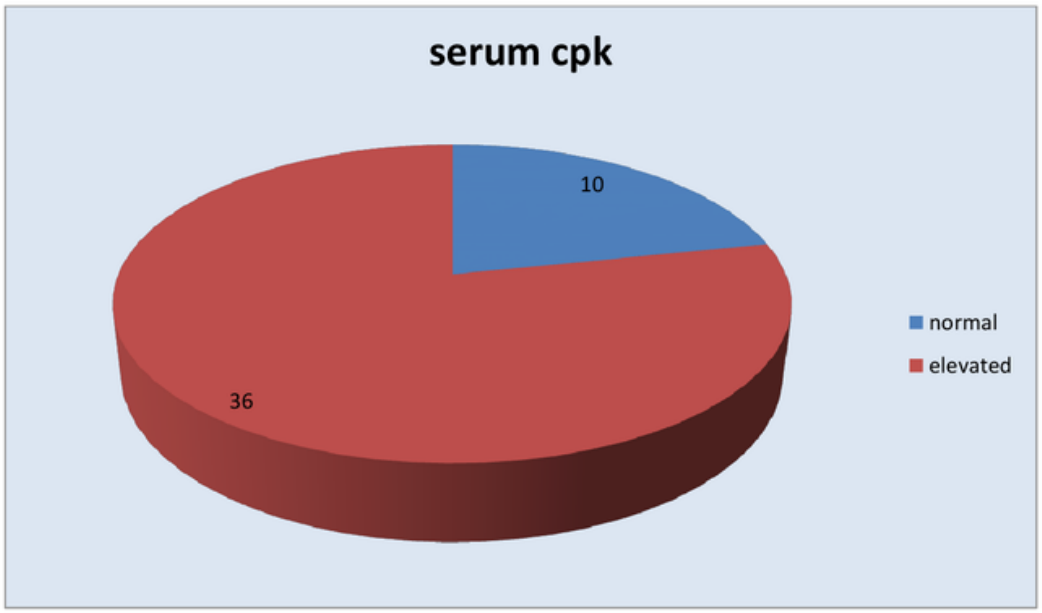
Serum Creatinine of more than 1.5 mg% was the cut off for terming elevated creatinine value.

Serum Creatinine

Serum Creatinine	No. of Patients
Less than or equal to 1.5 mg%	19
1.6 to 3.0 mg%	16
3.1 to 4.5 mg%	4
More than 4.5 %	7



Serum CPK(total) levels



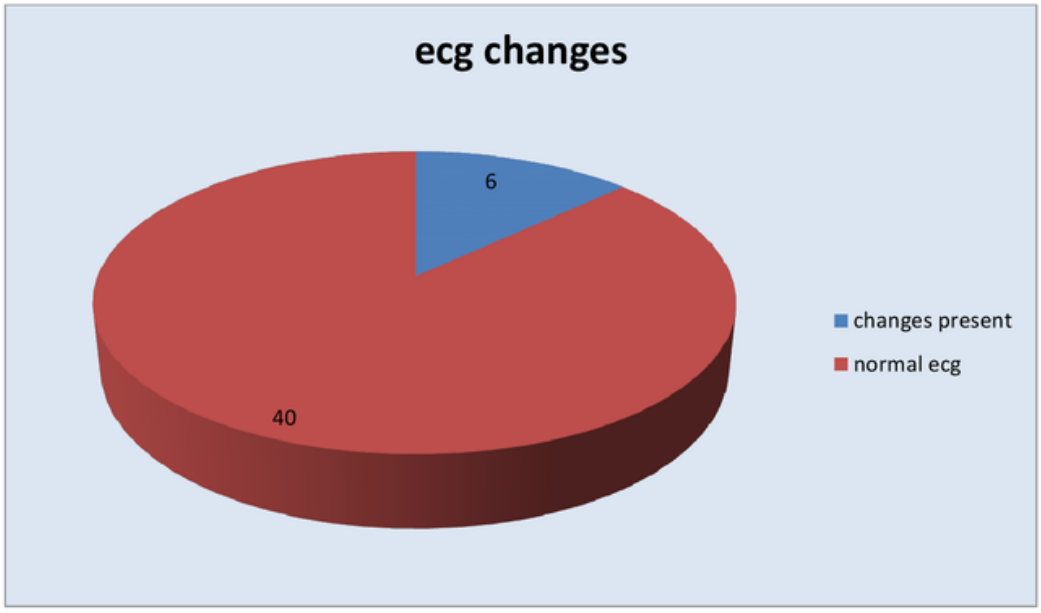
Serum total Creatine Phosphokinase levels were elevated in 78% of the patients. It ranged from 434 u/l to 2100 u/l; values gradually decreased in majority of patients with establishment of normovolemic status with iv fluids and forced alkaline diuresis.

Cardiac Involvement

ECG changes

Six out of 46 patients had ecg changes (13.06%). Two patients had sinus tachycardia. Two had ST and T inversion. They had normal cardiac troponin T levels. They survived.

Only one patient, a 19 year old female, who was on hemodialysis for renal failure, had tachycardia with ventricular premature complexes on the 5th day of admission. By then she had hypotension which prompted us to take a repeat ecg, whose admission ecg was normal. Her cardiac troponin T was positive (> 0.1 ng/ml), she was put on ventilator because she had hypoxia – she eventually expired; echocardiogram was not taken since the patient couldn't be shifted.



Treatment Details

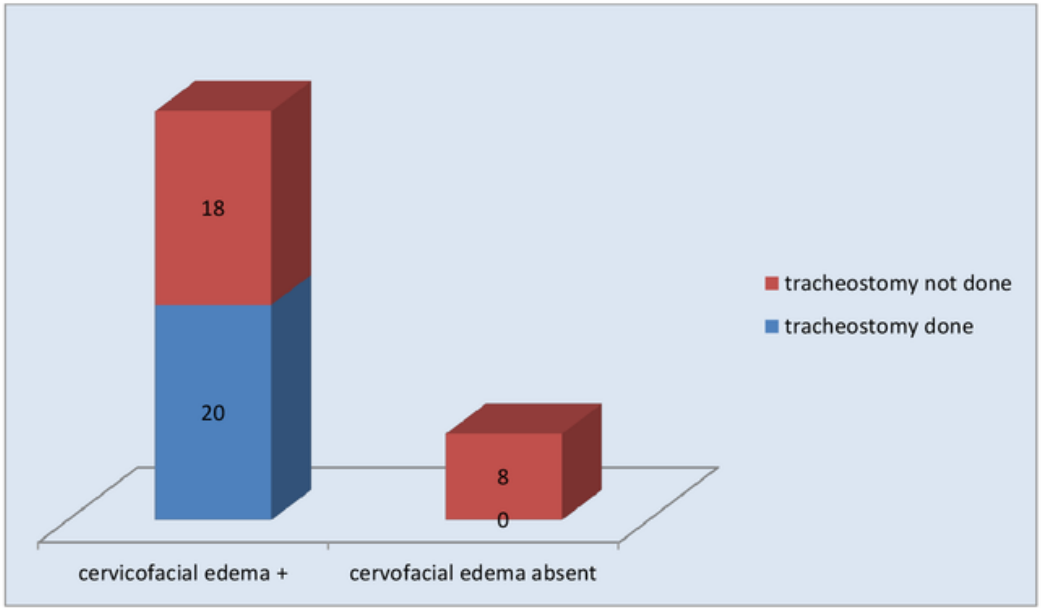
STEROIDS

All patients were administered Inj Hydrocortisone 200 mg iv stat on admission followed by 100 mg iv 6th hourly. The duration of treatment was for a maximum of five days. Some patients who had no cervicofacial edema at admission and upto 24 hours of admission were given intravenous steroid for one to three days only.

TRACHEOSTOMY

	Tracheostomy done	Tracheostomy not done
Cervicofacial edema present	20	18
Cervicofacial edema absent	-	8

Out of 38 patients who had edema of the face, neck, tongue, pharynx etc., only 20 patients required tracheostomy.



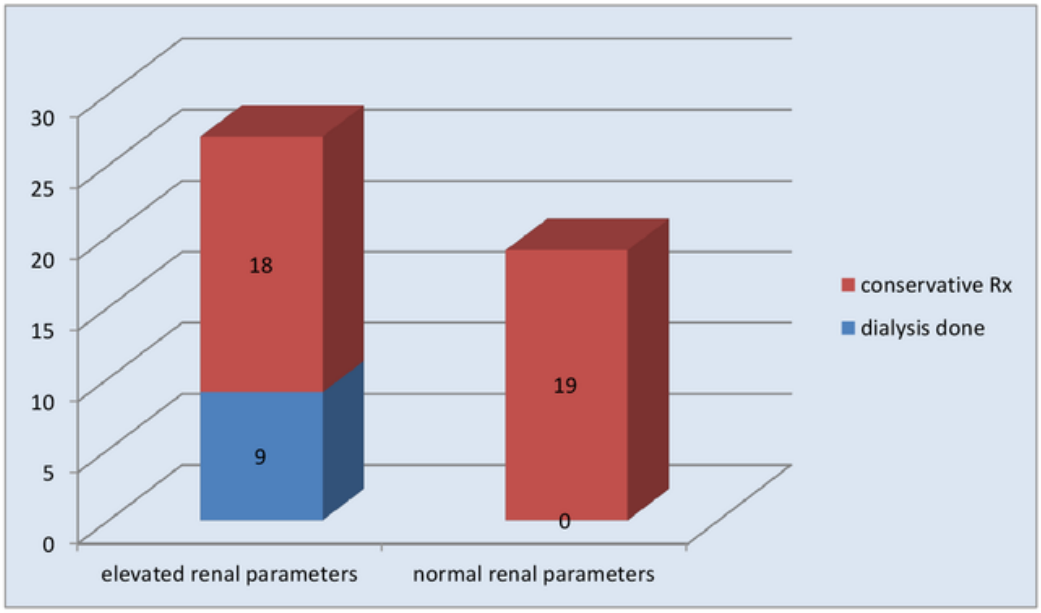
MECHANICAL VENTILATION

Only two patients required mechanical ventilator support. One of them had myocarditis and renal failure. Another patient had renal failure and required ventilator support towards the end of life. Both patients expired.

HEMODIALYSIS

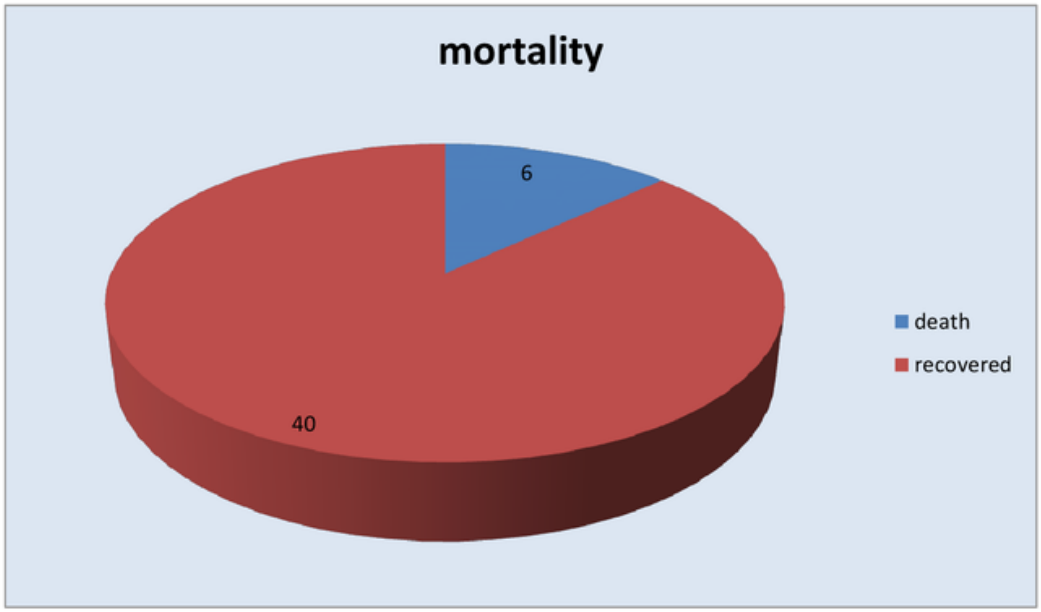
Hemodialysis was required in nine of the 27 patients who had elevated renal parameters. Eighteen patients were managed conservatively with high rate of fluid infusion along with forced alkaline diuresis to facilitate/accelerate the clearance of myoglobin. Nine patients who had rising serum creatinine values, not decreasing by conservative measures, had to undergo hemodialysis. Out of the nine patients, six patients died. One of them had developed myocarditis during the course of hospital stay.

	Hemodialysis	Conservative management	Total
Patients with elevated renal parameters	9	18	27



OUTCOME

Outcome	No. of Cases	Percentage
Recovered	40	86.95%
Expired	6	13.05%



Analysis of Outcome vs Other factors

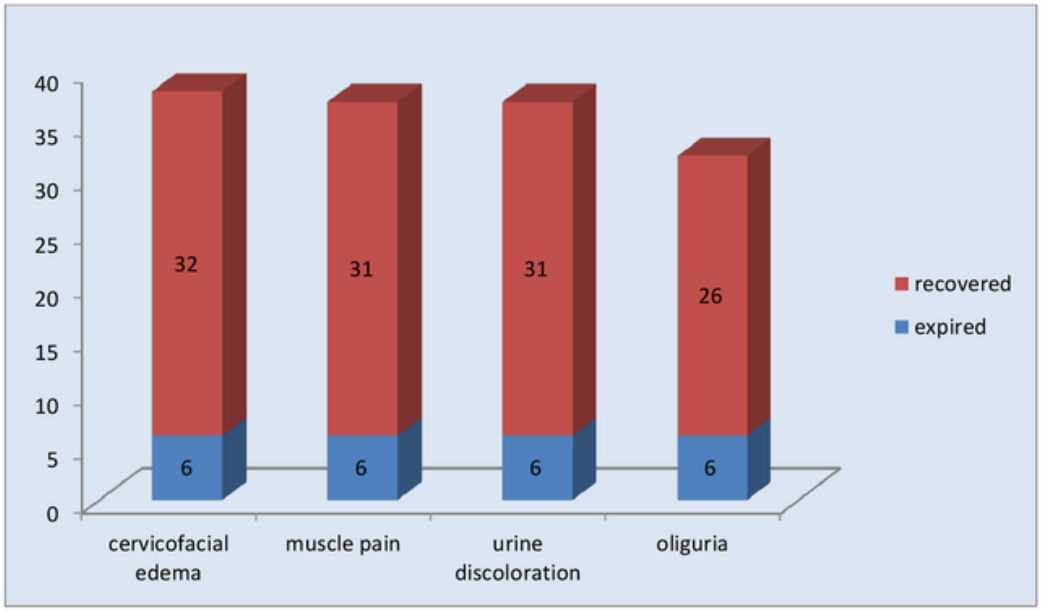
Gender and Outcome

	Total no. of cases	Death	Percentage
Male	16	2	12.50%
Female	30	4	16.67%

The mortality rate was more among females (16.67%) than in males.

Clinical Features and Outcome

Cervicofacial edema, dark colored urine, muscle pain and oliguria were present in all the six expired cases. Most of the patients who had these features recovered.



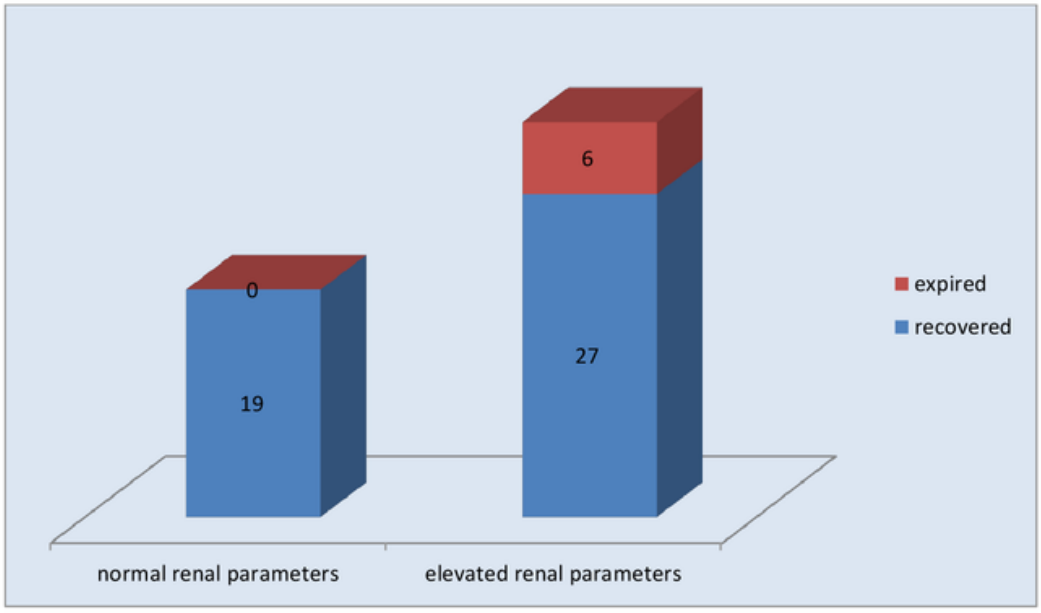
Seizures and Outcome

Only one patient had seizures and she expired. The patient also had renal failure and was on renal replacement therapy.

Renal Failure and Outcome

All patients who expired had elevated serum creatinine levels. Five of them were on renal replacement therapy (hemodialysis). One of them had myocarditis, evidenced by ecg changes and positive cardiac troponin T.

Serum Creatinine	No. of Patients	Death
Less than or equal to 1.5 mg%	19	-
1.6 to 3.0 mg%	16	-
3.1 to 4.5 mg%	4	1
More than 4.5 %	7	5



All 19 patients who had normal renal parameters recovered.

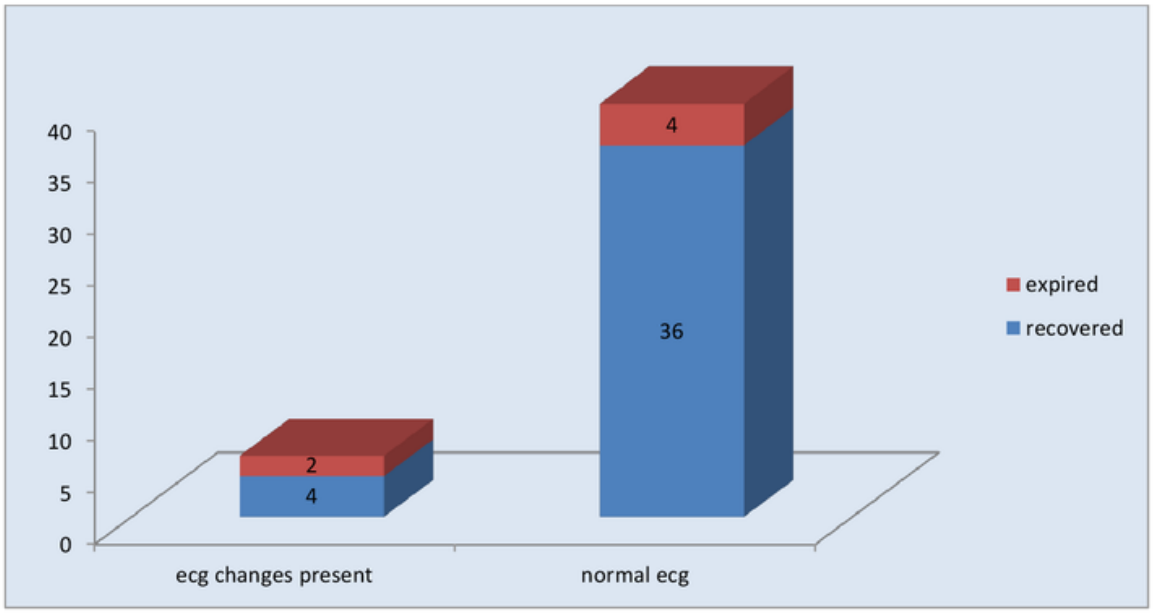
Among the 27 patients who had elevated serum creatinine, six patients, ie., 23% expired. All patients who had creatinine in the range of 1.6 mg% to 3.0 mg% recovered. Among the seven patients who had creatinine more than 4.5 mg%, five expired.

Ecg changes and Outcome

Out of the six patients who had ecg changes, 3 were males, 3 were females. Two patients, one male and one female expired. One of them, a

female patient had tachycardia, irregular rhythm, T inversion, had myocarditis evidenced by positive cardiac troponin T.

Out of the six patients who expired, two had ecg changes.



The Need For Ventilator Support And Outcome

Two patients required ventilator support for a period of more than 6 hours. Both of them expired. One of them, a female, had renal failure and myocarditis, as evidenced by positive cardiac troponin T. She had tracheostomy.

Another person, a male, had tracheostomy for airway management, had elevated renal parameters which was coming down on conservative management (iv fluids and alkaline diuresis), had hypotension; his ecg had sinus tachycardia, his cardiac troponinT was negative.

DURATION OF STAY AND OUTCOME

The duration of hospital stay was directly proportional to the complications and interventions. The average duration of stay was five to seven days for those who were managed totally conservatively for airway edema, renal failure etc. For those who had tracheostomy, and without hemodialysis for elevated renal parameters, the duration of stay was 7 to 10 days. For those who had renal failure and on hemodialysis, two to three weeks stay was required to recover from the illness.

DISCUSSION

6. DISCUSSION

Hair dye poisoning, first documented in 1924, is emerging as one of the common household agents used for deliberate self harm. The ease of availability, nominal cost, ease of mode of consumption all make this compound an attractive one for suicidal attempts.

The active ingredient – paraphenylenediamine is responsible for almost all the complications of hair dye ingestion namely, angioedema, rhabdomyolysis, renal failure, myocarditis etc.

Since there is no antidote, early recognition of the condition along with institution of early treatment is very important to ensure a good outcome. In our study, 93.4 % of individuals consumed the hair dye with an intention of self harm. Only a meagre percentage consumed it accidentally. This rate was consistent with the findings of PKJain et al (97.84%) [8], in a study comprising large number of patients in North India. All those who consumed it accidentally recovered, since they may have stopped consuming the product on recognition that they're consuming an unpalatable thing. These patients recovered with conservative measures.

Regarding the age group, 15 to 35 years age group comprised nearly 80% of the total number of patients, which is consistent with the findings of PKJain et al [8] and Raghu Kondle et al[41]. The majority of patients were females 66% in our study which is also consistent with the findings of various studies done in India. [8,41,].

Cervicofacial edema was present in majority (80%) of the patients in our study which is consistent with the findings of PK Jain et al (73%)[8] , Raghu Kondle et al (88%)[41] and Salma Mohamed et al(100%)[42]. Urinary discoloration was present in 80% of patients in our study; it was present in 94% and 47% respectively in studies conducted by Raghu Kondle et al[8] and PK Jain et al[41] respectively.

Seizures were present in 2.17% patients in our study. The rate was comparable with studies published in JCMR [8,]. Oliguria was present in 69% in our study; oliguria was present in 100% cases in study by Manisha Sahay et al, and 25% in PK Jain et al study. Hypotension was present in 15.21% of patients in our study which is comparable with findings of PK Jain et al (14.61%)[8].

Serum Creatinine was elevated in 58.69% patients in our study. The rate was 25.6% in JCMR study[8], 60% in Salma Mohamed Suliman etal

study[42]. Serum Cpk was elevated in 78.2% in our study and it was 58.3% in PK Jain et al study[8].

Steroids was started for all patients on admission and given for five days for those with moderate to severe angioedema. Only 52.63% of patients who had airway edema required tracheostomy. Among the patients who had elevated serum creatinine, only nine(33.33%) of them required dialysis.

The mortality rate was almost similar in males anad females in our study (12.5% and 16.67% respectively). Overall mortality was 13.05% in our study and 22.48% in PK Jain et al study. The mortality rate was lower among patients who received methyl prednisolone (14.02%) compared to hydrocortisone(27.7%)in that study[8]. In our study only hydrocortisone was used.

Of the total six cases who expired, all of them had angioedema requiring tracheostomy; all had muscle pain, elevated creatine kinase and discolored urine; all of them had oliguria and elevated renal parameters, five of them were on dialysis, one patient had myocarditis. Ventilatory support was required for two patients.

CONCLUSION

7. CONCLUSION

Hair dye poisoning, an emerging cause of self harm among people in our region, is well poised to overtake the traditional modes of self harm and become the leading cause of suicides in our part of the world in the years to come. Since it was first published in 1996 in the Journal of Association of Physicians of India, the incidence is steadily increasing, with significant mortality and morbidity.

A unique feature of this poisoning is the absence of antidote when compared to other 'traditional' modes of poisoning like insecticides etc. Therefore, the key is to recognize this condition earlier, start supportive therapy to ensure good outcome.

The short term prognosis was determined by respiratory failure due to airway edema. The long term prognosis is related to muscular and renal damage. In the primary care set up itself, attempts can be made to mitigate the future damage, if measures like steroids and parenteral liberal fluid therapy was started before referring the patient to higher centres. Thus the knowledge about this condition should be imparted to all primary care physicians of our country.

In higher centres, apart from maintaining the airway, efforts should be taken to prevent renal failure by fluid therapy, alkaline diuresis etc. since it was found in our study and many other studies that renal failure once established, is associated with high mortality.

There is a strong case for the ban of the sale of hair dye and other cosmetic products containing paraphenylene diamine and regulation of products containing paraphenylene diamine for industrial use, since it is inexpensive, easily accessible, omnipresent, has the potential to cause significant mortality and morbidity among all sections of people, especially children who may consume it accidentally, leading to social problems. Instead, dyes containing products other than paraphenylenediamine should be promoted.

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BIBLIOGRAPHY

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APPENDIX

PROFORMA

Name | Date of admission

Age | Date of discharge/death

Gender | IP no.

Address

Exclusion

1. Doesn't opt for inclusion in the study
2. Death within 6 hrs of admission
3. Absconded within 24 hrs
4. Known cardiac patient
5. Known renal disease patient

- Date, time of consumption
- Date, time of admission
- Product (hair dye) name & form :
- Amount consumed :

- Circumstance of consumption : Suicidal/intentional ; accidental

SYMPTOM PROFILE

1. Face, neck, tongue swelling
2. Dysphagia
3. Discolored urine
4. Oliguria
5. Limb pain
6. Dyspnea
7. Chest pain
8. Voice change (nasal twang/ dysphonia)
9. Convulsions
10. Syncope

SIGNS

1. Tachycardia
2. Tachypnea
3. Hypotension /Hypertension
4. Oliguria
5. Altered sensorium
6. Oxygen saturation
7. Angioedema

8. LIMBS Swelling

   Tenderness

   Stiffness

9. Chest pain

   Palpitation

   Syncope

   Dyspnea on exertion/ at rest

INVESTIGATIONS

1. Blood TC

   DC

2. ESR
3. URINE Alb Sugar Deposits
4. Blood Sugar
5. Blood Urea
6. Serum Creatinine
7. Serum Na^+ K^+ Ca^{++} HCO^-_3 Cl
8. Serum CPK
9. ECG { T↓ ; ST ↑ ; ST ↓ ; BBB ;

   VPCs ; AF ; VT }

10. LFT { S. bilirubin ; SGOT ;SGPT ;ALP }

For those with clinical and ECG evidence of myocarditis

- Troponin T

TREATMENT

1. STEROIDS Drug used

   Duration
2. Tracheostomy
3. Forced Alkaline Diuresis
4. Dialysis
5. Others – inotropes, antiarrhythmics etc.

OUTCOME

1. Recovered completely
2. Residual damage – renal/ cardiac/ others
3. Death – probable cause :

ANALYSIS

1. Age
2. Gender

3. Compound ingested

4. Intentional/ Accidental

5. *Clinical/lab* - Airway compromise

   Rhabdomyolysis

   Renal failure, dialysis

   Myocarditis

6. Mortality rate

MASTER CHART

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	19	F	I	Y	Y	Y	Y	N	N	N	Y	E	E	E	N		Y	N	Y	N	D
2	22	F	I	N	N	Y	N	N	N	N	N	N	E	N	N		Y	N	N	N	A
3	25	F	I	Y	Y	Y	Y	N	N	N	Y	E	N	N	N		N	N	N	N	A
4	48	M	I	Y	Y	Y	Y	N	Y	N	N	N	E	E	P	N	N	N	N	N	A
5	26	F	I	Y	Y	Y	Y	Y	N	Y	Y	E	E	N	N		Y	Y	Y	Y	D
6	17	F	I	Y	Y	Y	Y	N	N	N	Y	E	E	N	N		N	N	Y	N	A
7	24	F	I	Y	Y	Y	Y	N	N	N	N	N	E	N	N		N	N	N	N	A
8	36	M	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		Y	N	N	N	A
9	18	F	I	N	N	N	N	N	N	N	N	N	N	N	N		N	N	N	N	A
10	20	M	I	Y	Y	Y	Y	Y	Y	N	Y	E	E	E	P	N	N	N	Y	N	A
11	37	F	I	Y	Y	N	Y	N	N	N	N	N	E	N	N		N	N	N	N	A
12	19	F	I	Y	Y	Y	N	N	N	N	N	N	E	E	N		N	N	N	N	A
13	27	M	I	Y	Y	Y	Y	Y	N	N	Y	E	E	N	N		Y	N	Y	Y	D
14	20	F	I	Y	N	Y	N	N	N	N	N	E	E	E	N		Y	N	N	N	A
15	20	F	I	Y	Y	Y	Y	N	Y	N	N	N	N	N	P	N	N	N	N	N	A
16	27	M	A	Y	Y	N	N	N	N	N	N	N	E	N	N		N	N	N	N	A
17	21	F	I	Y	Y	Y	Y	N	N	N	Y	E	E	E	N		Y	N	N	N	A
18	46	F	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		N	N	N	N	A
19	23	F	I	N	N	Y	N	N	N	N	Y	N	E	N	N		N	N	N	N	A
20	21	M	I	Y	Y	Y	Y	N	N	N	Y	E	N	N	N		Y	N	N	N	A
21	27	F	I	Y	Y	N	N	N	N	N	N	E	E	E	N		N	N	N	N	A
22	19	M	I	Y	Y	Y	Y	Y	Y	N	Y	E	E	E	P	N	N	N	N	Y	D
23	40	F	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		Y	N	N	N	A
24	24	M	I	Y	Y	N	Y	N	N	N	N	N	E	N	N		N	N	N	N	A
25	22	F	I	Y	Y	Y	Y	N	N	N	N	E	E	E	N		Y	N	N	N	A
26	30	M	I	Y	Y	Y	Y	N	N	N	N	N	N	N	N		Y	N	N	N	A
27	23	F	A	Y	Y	N	N	Y	Y	N	Y	E	E	E	P	N	Y	N	N	N	A
28	33	F	A	Y	Y	Y	Y	N	N	N	N	E	E	N	N		N	N	N	N	A
29	45	F	I	Y	Y	Y	Y	N	N	N	Y	N	E	E	N		N	N	N	N	A
30	24	M	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		N	N	N	N	A
31	17	F	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		Y	N	N	N	A
32	29	M	I	N	N	N	N	N	N	N	N	N	N	N	N		N	N	N	N	A
33	32	F	I	Y	Y	Y	Y	N	N	N	Y	E	E	N	N		Y	N	N	N	A
34	30	F	I	Y	Y	Y	Y	N	N	N	Y	E	E	N	N		N	N	Y	N	A
35	22	F	I	Y	Y	Y	Y	N	N	N	Y	N	E	E	N		N	N	N	N	A
36	34	M	I	Y	Y	Y	Y	N	N	N	N	N	E	N	N		Y	N	N	N	A
37	29	F	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		Y	N	N	N	A
38	43	F	I	N	N	N	N	N	N	N	N	N	N	N	N		N	N	N	N	A
39	33	M	I	Y	Y	Y	Y	N	N	N	Y	E	E	E	N		Y	N	N	N	A
40	19	F	I	Y	Y	Y	Y	Y	N	N	Y	E	E	E	P	E	Y	Y	Y	Y	G
41	33	M	I	Y	Y	Y	Y	N	N	N	N	E	E	N	N		N	N	N	N	A
42	25	F	I	Y	Y	Y	Y	N	Y	N	Y	E	E	N	N		Y	N	Y	N	A
43	26	M	I	Y	Y	Y	N	N	N	N	N	N	E	N	N		N	N	N	N	A
44	20	F	I	Y	Y	Y	Y	Y	N	N	Y	E	E	E	N		Y	N	Y	N	D
45	35	M	I	N	N	N	N	N	N	N	N	N	N	N	N		N	N	N	N	A
46	46	F	I	N	N	Y	N	N	N	N	Y	N	N	N	N		N	N	N	N	A

ABBREVIATIONS

A age

B sex

M male

F female

C circumstance of the poisoning

I intentional

A accidental

D cervicofacial edema

Y present

N absent

E limb pain/swelling

Y present

N absent

F urine discoloration

Y present

N absent

G oliguria

Y present

N absent

H hypotension

Y present

N absent

I tachypnea, dyspnea

Y present

N absent

J seizures

Y present

N absent

K proteinuria

Y present

N absent

L creatinine elevation > 1.5 mg%

E elevated

N normal

M CPK elevation

E elevated

N normal

N SGOT, SGPT elevation

E elevated

N normal

O ECG changes

N normal

P present

P Troponin T

NL normal

E elevated

Q tracheostomy

Y done

N not done

R mechanical ventilation

Y required

N not required

S dialysis

Y done

N not done

T inotrope use

Y used

N not indicated/used

U outcome

D dead

A alive